

REMARKS

The present Preliminary Amendment enters an initial paper copy of a Sequence Listing into the application in accordance with 37 C.F.R. §§ 1.821-1.825. The initial Sequence Listing identifies the nucleotide and/or amino acid sequences originally disclosed in the application.

Further, a computer readable form of the Sequence Listing in accordance with the requirements of 37 C.F.R. § 1.824 is herewith submitted.

STATEMENT UNDER 37 C.F.R. § 1.821

Applicant's representative submits the following Statement under 37 C.F.R. § 1.821(f): Applicant's undersigned representative hereby states that the content of the Sequence Listing of the above-captioned patent application, and the computer readable copy filed herewith on a computer disk are believed to be the same. Applicant's representative further states that the Sequence Listing adds no new matter to the application.

The present Preliminary Amendment also amends the specification to coordinate the SEQ ID NOS with the order they are set forth in the sequence listing and to correct obvious minor typographical errors and. In particular, new SEQ ID NOS. are given to the amino acid constructions referred to in Table B (page 28), Table G (page 30), Table 13 (pages 78-79), Table 18 (page 85) and Table 22 (pages 89-90). Further, the text within the columns named "Protein designation" and "Identification" of Table 2, although present, was not fully visible due to formatting errors within the cells of the columns. Likewise, the text within the cells of the first row of Table 23 containing the column headings also was not fully visible due to formatting errors. Applicants amend these Tables so that the text within the cells is visible. Applicants

submit that the information was indeed present in the original text and that the formatting errors are obvious and typographical in nature. No new matter is added in the application.

Attached hereto is a marked-up version of the changes made to the drawings by the current amendment. The changes to the drawings are underlined and appear in bold type. The attached page is captioned "Version With Markings To Show Changes Made."

In addition, hereto is an attached paper copy of the substitute Sequence Listing. The paper copy and computer readable copy of the substitute Sequence Listing are the same. The substitute Sequence Listing does not include new matter.

CONCLUSION

Entry of the Preliminary Amendment and Sequence Listing and favorable consideration are respectfully requested.

To the extent necessary, please grant any extension of time deemed necessary for entry of this communication. Please charge any deficient fees, or credit any overpayment of fees, to Deposit Account 500417.

Respectfully submitted,

McDermott, Will & Emery



Kelli N. Watson

Registration No. 47,170

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McDermott, Will & Emery
600 Thirteenth Street, N.W.
Washington, D.C. 20005-3096
(202) 756-8351 (direct)
(202) 756-8087 (fax)

ATTACHMENT
Version With Markings To Show Changes Made

IN THE SPECIFICATION

Table B on pages 28 has been substituted with the following rewritten Table B in its place.

--TABLE B --

Family	Polypeptide SEQ ID NO.
BVH-3	
NEW1-mut1**	237
NEW35A	238
NEW42	[237] <u>349</u>
NEW49	[238] <u>350</u>
NEW50	[239] <u>351</u>
NEW51	[240] <u>352</u>
NEW52	[241] <u>353</u>
NEW53	[242] <u>354</u>
NEW54	[243] <u>355</u>
NEW55	[244] <u>356</u>
NEW56	[245] <u>357</u>
NEW56-mut2**	[245] <u>358</u>
NEW56-mut3**	[245] <u>359</u>
NEW57	[246] <u>360</u>
NEW63	[247] <u>361</u>
NEW64	[248] <u>362</u>
NEW65	[249] <u>363</u>
NEW66	[250] <u>364</u>
NEW76	[251] <u>365</u>
NEW105	[252] <u>366</u>
NEW106	[253] <u>367</u>
NEW107	[254] <u>368</u>

** silent mutation, i.e. the polypeptide is the same as New1 or New 56

Table G on page 30 has been substituted with the following rewritten Table G in its place.

-- TABLE G

Family	Polypeptide SEQ ID NO
Chimeras with BVH-11 and BVH-3	
New17	M*-NEW5-G*P*-NEW1 (376)
New20	M*-NEW1-G*P*-NEW5 (377)
New26	M*-NEW10-G*P*-NEW25 (378)
New27	M*-NEW19-G*P*-NEW25 (379)
New28	M*-NEW10-G*P*-NEW1 (380)
New29	M*-NEW5-G*P*-NEW25 (381)
New30	M*-NEW4-G*P*-NEW25 (382)
New31	M*-NEW4-G*P*-NEW1 (383)
NEW32	M*-NEW19-G*P*-NEW1 (384)

* OPTIONAL AMINO ACID--

Table 2 on pages 38 and 39 has been substituted with the following Table 2 in its place.

-- Table 2. Lists of truncated BVH-3, BVH-11, BVH-11-2 and Chimeric gene products generated from S. pneumoniae SP64

PCR-primer sets	Protein designation	Identification	Encoded amino acids (SEQ ID No6)	Cloning vector
OCRR479-OCRR480	BVH-3M	BVH-3 w/o ss	21-1039	pSL301
OCRR479-OCRR497	BVH-3AD	BVH-3 N'end w/o ss	21-509	pSL301
HAMJ248-HAMJ249	L-BVH-3AD	BVH-3 N'end	1-509	pET-21(+)
OCRR498-OCRR499	BVH-3B	BVH-3 C'end	512-1039	pSL301
OCRR479-HAMJ172	BVH-3C	BVH-3 N'end w/o ss	21-225	pET-32 c(+)
OCRR487-OCRR488	BVH-11M	BVH-11 w/o ss	20-840	pCMV-GH
HAMJ251-OCRR487	BVH-11A	BVH-11 N'end w/o ss	20-353	pET-32 c(+)
HAMJ171-OCRR488	BVH-11B	BVH-11 C'end	354-840	pET-32 a(+)
HAMJ264-OCRR488	BVH-11C	BVH-11 C'end	228-840	pET-32 a(+)
HAMJ278-HAMJ279	NEW1	BVH-3 C'end	472-1039	pET-21b(+)
HAMJ278-HAMJ280	NEW2	BVH-3 C'end	472-800	pET-21b(+)
HAMJ281-HAMJ279	NEW3	BVH-3 C'end	800-1039	pET-21b(+)
HAMJ284-HAMJ285	NEW4	BVH-11 C'end	286-840	pET-21d(+)

HAMJ284-HAMJ286	NEW5	BVH-11 internal	286-713	pET-21d(+)
HAMJ287-HAMJ288	NEW6	BVH-11 internal	672-792	pET-21d(+)
HAMJ285-HAMJ289	NEW7	BVH-11 C'end	709-840	pET-21d(+)
HAMJ284-HAMJ290	NEW8	BVH-11 internal	286-511	pET-21d(+)
HAMJ286-HAMJ291	NEW9	BVH-11 internal	511-713	pET-21d(+)
HAMJ160-HAMJ186	BVH-11-2M	BVH-11-2 w/o ss	20-838	pSL301
HAMJ292-HAMJ293	NEW10	BVH-11-2 C'end	271-838	pET-21d(+)
HAMJ293-HAMJ294	NEW11	BVH-11-2 C'end	699-838	pET-21d(+)
HAMJ282-HAMJ283	NEW13	BVH-11 C'end	354-840	pET-21b(+)
HAMJ286-HAMJ297	NEW14	BVH-11-2 internal	227-699	pET-21d(+)
HAMJ300-HAMJ313	NEW15	BVH-3 N'end w/o ss	21-800	pET-21b(+)
HAMJ301-HAMJ302	NEW16	BVH-11 N'end w/o ss	20-709	pET-21d(+)
HAMJ352-HAMJ353	NEW18	BVH-11-2 internal	227-520	pET21d(+)
HAMJ354-HAMJ355	NEW19	BVH-11-2 C'end	497-838	pET21d(+)
HAMJ404-HAMJ279	NEW21	BVH-3 C'end	396-1039	pET21b(+)
HAMJ464-HAMJ465	NEW22	BVH-3 internal	233-446	pET-21a(+)
HAMJ466-HAMJ467	NEW23	BVH-3 internal	398-509	pET-21b(+)
HAMJ352-HAMJ293	NEW24	BVH-11-2 C'end	227-838	pET-21d(+)
HAMJ464-HAMJ470	NEW25	BVH-3 C'end	233-1039	pET-21b(+)
HAMJ278-HAMJ279 (NEW 1) HAMJ282- HAMJ283 (NEW 13)	NEW12	Chimera*	M-NEW 1 -KL - NEW 13	pET 21 b (+)
HAMJ284-HAMJ350 (NEW 5) HAMJ351- HAMJ279 (NEW 1)	NEW17	Chimera*	M- NEW 5 -GP - NEW 1	pET 21 d (+)
HAMJ358-HAMJ359 (NEW 1) HAMJ403- HAMJ361 (NEW 5)	NEW20	Chimera*	M- NEW 1 -GP - NEW 5	pET 21 d (+)
HAMJ292-HAMJ471 (NEW 10) HAMJ472- HAMJ470 (NEW 25)	NEW26	Chimera*	M- NEW 10 -GP - NEW 25	pET 21 d (+)
HAMJ355-HAMJ471 (NEW 19) HAMJ472- HAMJ470 (NEW 25)	NEW27	Chimera*	M- NEW 19 -GP - NEW 25	pET 21 d (+)
HAMJ292-HAMJ471 (NEW 10) HAMJ351 - HAMJ279 (NEW 1)	NEW28	Chimera*	M- NEW 10 -GP - NEW 1	pET 21 d (+)
HAMJ284-HAMJ350 (NEW 5) HAMJ472- HAMJ470 (NEW 25)	NEW29	Chimera*	M- NEW 5 -GP - NEW 25	pET 21 d (+)
HAMJ284-HAMJ483 (NEW 4) HAMJ472- HAMJ470 (NEW 25)	NEW30	Chimera*	M- NEW 4 -GP - NEW 25	pET 21 d (+)

HAMJ284-HAMJ483 (NEW 4) HAMJ351- HAMJ279 (NEW 1)	NEW31	Chimera*	M- NEW 4 -GP - NEW 1	pET 21 d (+)
HAMJ355-HAMJ471 (NEW 19) HAMJ351- HAMJ279 (NEW 1)	NEW32	Chimera*	M- NEW 19 -GP - NEW 1	pET 21 d (+)

w/o ss : without signal sequence. Analysis of the BVH-3, BVH-11 and BVH-11-2 protein sequences suggested the presence of putative hydrophobic leader sequences.

* encoded amino acids for the chimeras are expressed as the gene product, additional non essential amino acids residue were added M is methionine, K is lysine, L is leucine, G is glycine and P is proline.-

Table 13 on pages 78 and 79 has been substituted with the following rewritten Table 13 in its place.

-- Table 13. Lists of truncated variant BVH-3 gene products generated from S. pneumoniae SP64

Prot in designation	Gene/ Protein SEQ ID NO	Protein Identification*	PCR primer set (ref. table 12)	Gene used for mutagenesis
NEW1 - mut1**	[237]255	NEW1	39	NEW1
NEW35A	[238]256	NEW1 550- <u>SGD</u> <u>GTS</u> -555	14,17,20,22	NEW1
NEW42	[239]349	NEW40 55- <u>SGD</u> <u>SN</u> <u>S</u> -60 144- <u>SGD</u> <u>GTS</u> -149	9, 10, 11, 14, 17, 20, 22	NEW40
NEW49	[240]350	NEW40 55- <u>SGD</u> <u>HNH</u> -60	9	NEW40
NEW50	[241]351	NEW40 55- <u>SGD</u> <u>SNH</u> -60	10	NEW49
NEW51	[242]352	NEW40 55- <u>SGD</u> <u>HNH</u> -60 144- <u>SGD</u> <u>HHH</u> -149	14	NEW49
NEW52	[243]353	NEW40 55- <u>SGD</u> <u>SNH</u> -60 144- <u>SGD</u> <u>GHH</u> -149	10, 17	NEW51
NEW53	[244]354	NEW40 55- <u>HGD</u> <u>HNH</u> -60 144- <u>SGD</u> <u>HHH</u> -149	14	NEW40
NEW54	[245]355	NEW40 55-[S] <u>HGD</u> <u>HNH</u> -60 144- <u>SGD</u> <u>GHH</u> -149	17	NEW53
NEW55	[246]356	NEW1 550- <u>HGD</u> <u>GHH</u> -555	23	NEW1
NEW56	[247]357	NEW40 55- <u>HGD</u> <u>SNH</u> -60 144- <u>SGD</u> <u>HHH</u> -149	24	NEW53
NEW56 - mut2**	[248]358	NEW56	40	NEW56
NEW56 - mut3**	[249]359	NEW56	46,47,48	NEW56
NEW57	[250]360	NEW40 55- <u>HGD</u> <u>HNS</u> -60 144- <u>SGD</u> <u>HHH</u> -149	25	NEW53
NEW63	[251]361	NEW40 55- <u>HGD</u> <u>SNH</u> -60 144- <u>HGD</u> <u>HHH</u> -149	24	NEW40
NEW64	[252]362	NEW40 55- <u>HGD</u> <u>HNS</u> -60 144- <u>HGD</u> <u>HHH</u> -149	25	NEW40
NEW65	[253]363	NEW40 55- <u>HGD</u> <u>SNH</u> -60 144- <u>HGD</u> <u>GHH</u> -149	23	NEW63

Protein designation	Gene/ Protein SEQ ID NO	Protein Identification*	PCR primer set (ref. table 12)	Gene used for mutagenesis
NEW66	[254]364	NEW40 55-HGDHNS-60 144-HGDGHH-149	23	NEW64
NEW76	[255]365	NEW40 55-HGDHNS-60 144-SGDGHH-149	17	NEW64
NEW105	[256]366	NEW40 55-____-60	41, 42, 43	NEW40
NEW106	[257]367	New40 144-____-149	44, 45	NEW40
NEW107	[258]368	NEW40 55-____-60 144-____-149	44, 45	NEW105

* The underlined amino acid residues represent the modification in protein sequence. Nucleotides/amino acid residues are deleted in NEW105, NEW106 and NEW107 constructs.

** silent mutation, i.e. the polypeptide is the same as New1.-

Table 18 on page 85 has been substituted with the following Table 18 in its place.

-- Table 18. Properties of NEW86 and VP43S genes generated from NEW43 gene

PCR-primer sets	Gene/ Protein designation	Identification
HAMJ610-HAMJ354	VP43S	NEW43 C'end corresponding to residues 15-272) (<u>SEQ ID NO:374</u>)
HAMJ490-HAMJ583 HAMJ584-HAMJ354	NEW86	NEW43 109-__PG__-114 (<u>SEQ ID NO:375</u>)

Table 22 on pages 89 and 90 has been substituted with the following Table 22 in its place.

--Table 22. List of polypeptides encoded by chimeric genes comprising a BVH-3 truncate variant gene and a NEW43 or NEW43 variant gene

Polypeptide designation	SEQ ID NO	Identification
VP 89	[327] <u>369</u>	M-New56 -GP- New43*
VP 90	[328] <u>370</u>	M-New43 -GP- New56
VP 91	[329] <u>371</u>	M-New52 -GP- New43
VP 92	[330] <u>372</u>	M-New43 -GP- New52
VP 93	[331] <u>373</u>	M-New56 -GP- New60
VP 94	332	M-New60 -GP- New56
VP 108	333	M-New56 -GP- New88
VP109	334	M-New88 -GP- New56
VP 110	335	M-New60 -GP- New105
VP 111	336	M-New60 -GP- New107
VP112	337	M-New88 -GP- New105
VP113	338	M-New88 -GP- New107
VP114	339	M-New80-GP- New105

Polypeptide designation	SEQ ID NO	Identification
VP115	340	M-New80 -GP- New107
VP116	341	M-New83 -GP- New105
VP117	342	M-New83 -GP- New107
VP119	343	M-New43S- GP-New105
VP120	344	M-New43S- GP-New107
VP121	345	M-New80S- GP-New105
VP122	346	M-New80S- GP-New107
VP123	347	M-New88S- GP-New105
VP124	348	M-New88S- GP-New107

* Encoded amino acids for the chimeras are expressed as the gene product, additional amino acid residues were added. M is methionine, G is glycine and P is proline.--

Table 23 on page 91 has been substituted with the following Table 23 in its place.

Table 23. List of PCR oligonucleotide primer pairs designed for the generation of the chimeric genes encoding the polypeptides listed in Table 22.

Primer set	PCR-primer identification	Gene used for PCR amplification	Corresponding position of the gene fragment on the chimeric protein molecule
49	HAMJ490-HAMJ471	Variant New43	N-terminal
50	HAMJ564-HAMJ556	Variant New43	C-terminal
51	HAMJ489-HAMJ359	Variant New40	N-terminal
52	HAMJ559-HAMJ557	Variant New40	C-terminal
53	HAMJ610-HAMJ471	Variant New43S	N-terminal